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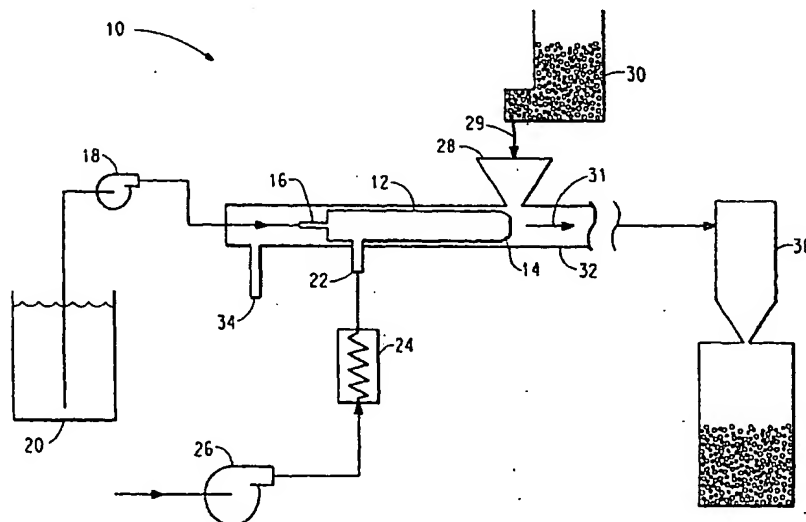
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: SOLID FLOWABLE POWDER WITH HIGH LIQUID LOADING



(57) Abstract: A process of manufacturing compositions comprised of carrier particles under 100 nm that have been loaded to a level of greater than 60% by weight with a liquid comprising metering the liquid into a flow restrictor, injecting a gas stream through the flow restrictor to atomize the liquid and create a zone of turbulence at the outlet end of a flow restrictor, and introducing particles through a hopper (28) into the zone of turbulence to mix the particles with atomized liquid thereby loading the particles with the liquid. The hopper (28) includes metering device for accurately metering the particles at a particular ratio to the liquid feed from liquid inlet line (16). The highly-liquid-loaded particles can be further coated or encapsulated with functional coating or encapsulating materials.

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**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**(88) Date of publication of the international search report:**

1 July 2004

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/25882

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : B05D 7/00

US CL : 427/2.15, 2.16, 212, 213

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 427/2.15, 2.16, 212, 213

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| Y          | US 5,681,577 A (LECH et al) 28 October 1997 (28.10.1997), column 3, lines 33-46.  | 2, 12, 15             |
| Y          | US 3,921,636 A (ZAFFARONI) 25 November 1975 (25.11.1975), column 7, lines 32-58, column 11, line 37, column 12, lines 27-37, 59-71. | 1-20                  |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

15 April 2004 (15.04.2004)

Date of mailing of the international search report

07 MAY 2004

Name and mailing address of the ISA/US

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Commissioner for Patents  
P.O. Box 1450  
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/25882**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

|                               |                            |     |
|-------------------------------|----------------------------|-----|
| Novelty (N)                   | Claims <u>9-13, 19, 20</u> | YES |
|                               | Claims <u>14, 15</u>       | NO  |
| Inventive Step (IS)           | Claims <u>1-8, 15-18</u>   | YES |
|                               | Claims <u>9-15, 19, 20</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-20</u>         | YES |
|                               | Claims <u>NONE</u>         | NO  |

**2. CITATIONS AND EXPLANATIONS**

Please See Continuation Sheet

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/25882

## Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1, 3-5, 8, 18 lack an inventive step under PCT Article 33(3) as being obvious over Zaffaroni (US 3,921,636) in view of Fujiura et al (US 5,002,986).

Zaffaroni further teach that pharmaceutical nanoparticles can be loaded using any known techniques (See column 7, lines 47-48). However, Zaffaroni fails to teach that the method is a method of claim 1.

Fujiura et al teach that high intensity mixing of liquid with fine particles can be performed in a fluid mixer by suspending fine particles in a turbulent gas stream and contacting them with a liquid sprayed from pressurized nozzles (See column 6, lines 54-66).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a method of Fujiura et al for mixing carrier particles with pharmaceuticals in Zaffaroni with the expectation of providing the desired high intensity mixing, as taught by Fujiura et al.

Claims 2, 6, 7 lack an inventive step under PCT Article 33(3) as being obvious over Zaffaroni (US 3,921,636) in view of Fujiura et al (US 5,002,986), further in view of Lech et al (US 5,681,577).

Zaffaroni in view of Fujiura et al, as applied above, fail to teach that essential fats are polyunsaturated fats (Claims 16, 17); the carrier is silica (Claims 15, 17).

It is well known in the art that essential fats are polyunsaturated fats including those of claim 17.

Lech et al teach that colloidal silica such as Cab-o-sil, can be used as a pharmaceutical carrier (See column 3, lines 33-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used colloidal silica as carrier and polyunsaturated fats as essential fats in Zaffaroni in view of Fujiura et al with the expectation of providing the desired loaded colloidal silica particles, since it is well known in the art that essential fats are polyunsaturated fats, including those of claim 17, and Lech et al teach that colloidal silica such as Cab-o-sil, can be used as a pharmaceutical carrier.

Claim 14 lacks novelty under PCT Article 33(2) as being anticipated by Handjani et al (US 6,203,802). Handjani et al disclose nanoparticles having size of 10-1000 nm (See column 3, lines 1-3), loaded with more than 60 wt % of oil (See column 3, lines 55-58) such as polyunsaturated fatty acid (See column 3, lines 46-48).

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/25882

## Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Claims 14, 15 lack novelty under PCT Article 33(2) as being anticipated by Lech et al (US 5,681,577). Lech et al disclose Cab-o-sil colloidal particles with dissolved drugs loaded or absorbed in an amount up to 99 % (See column 3, lines 33-51).

Claim 14 lacks an inventive step under PCT Article 33(3) as being obvious over Zaffaroni (US 3,921,636). Zaffaroni discloses nanoparticles of pharmaceutical carriers such as charcoal, calcium carbonate, starch, etc. having size of 5-7 nm (See column 12, lines 61-62), loaded or impregnated with any drug including essential fats (See column 11, line 37) using any known techniques (See column 7, lines 47-48). Zaffaroni fails to teach that: the amount of drug is greater than 60 %. However, one of ordinary skill in the art at would know that loaded amount would depend on absorbing ability of the carrier and particular drug used. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have loaded nanoparticles in Zaffaroni with the desired amount of drug including claimed amount of greater than 60 % of drug depending on particular carrier and drug.

Claims 15-17 lack an inventive step under PCT Article 33(3) as being obvious over Zaffaroni (US 3,921,636) in view of Lech et al (US 5,681,577).

Zaffaroni, as applied above, fails to teach that essential fats are polyunsaturated fats (Claims 16, 17); the carrier is silica (Claims 15, 17).

It is well known in the art that essential fats are polyunsaturated fats including those of claim 17.

Lech et al teach that colloidal silica such as Cab-o-sil, can be used as a pharmaceutical carrier (See column 3, lines 33-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used colloidal silica as carrier and polyunsaturated fats as essential fats in Zaffaroni with the expectation of providing the desired loaded colloidal silica particles, since it is well known in the art that essential fats are polyunsaturated fats, including those of claim 17, and Lech et al teach that colloidal silica such as Cab-o-sil, can be used as a pharmaceutical carrier.

Claims 1-20 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

## NEW CITATIONS

- US 6,203,802 A (HANDJANI et al) 20 March 2001, see column 3, lines 1-3, 25, 36-38, 55-58.  
US 5,002,986 (FUJIURA et al) 26 March 1991, see column 6, lines 54-66.

REC'D 12 JAN 2005

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|  |  |   |
|--|--|---|
| Applicant's or agent's file reference<br>CL2101PCT   | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |   |
| International application No.<br>PCT/US03/25882  | International filing date (day/month/year)<br>14 August 2003 (14.08.2003)  | Priority date (day/month/year)<br>14 August 2002 (14.08.2002) |
| International Patent Classification (IPC) or national classification and IPC<br>IPC(7): B05D 7/00 and US Cl.: 427/2.15, 2.16, 212, 213 |  |   |
| Applicant<br>E.I.DU PONT DE NEMOURS AND COMPANY  |  |   |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.  
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

|   |   |
|---|---|
| Date of submission of the demand<br>12 March 2004 (12.03.2004)  | Date of completion of this report<br>20 December 2004 (20.12.2004)        |
| Name and mailing address of the IPEA/US<br>Mail Stop PCT, Attn: IPEA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230 | Authorized officer<br><i>Shirley Beck</i><br>Telephone No. (703) 308-0661 |

Form PCT/IPEA/409 (cover sheet)(July 1998)

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/25882

## I. Basis of the report

## 1. With regard to the elements of the international application:\*



the international application as originally filed.



the description:

pages 1-21 as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of \_\_\_\_\_.



the claims:

pages 22-24, as originally filed

pages NONE, as amended (together with any statement) under Article 19

pages NONE, filed with the demand

pages NONE, filed with the letter of \_\_\_\_\_.



the drawings:

pages 1-2, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of \_\_\_\_\_.



the sequence listing part of the description:

pages NONE, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of \_\_\_\_\_.

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:



the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).



the language of publication of the international application (under Rule 48.3(b)).



the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:



contained in the international application in printed form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

the description, pages NONE



the claims, Nos. NONE



the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.